

LISTING OF CLAIMS

1. *(currently amended)* An isolated anti-angiogenic polypeptide that is:
 - (a) a variant of native HK-D3 (SEQ ID NO:1) designated HK-D3v which has the amino acid sequence [[()]]SEQ ID NO:3[()]], or
 - (b) a conservative amino acid substitution variant of SEQ ID NO:3, or (e) an N-terminal addition variant of native HK-D3 (SEQ ID NO:1), which has the sequence SEQ ID NO:2 is a conservative substitution variant, an N terminal addition variant of two amino acids and/or a substitution variant wherein a seven residue C terminal sequence is replaced,

which polypeptide or variant has at least 20% of the activity of native HK-D3 (SEQ ID NO:1) in inhibiting angiogenesis, endothelial cell proliferation or endothelial tube formation in an *in vitro* or *in vivo* bioassay.
3. *(previously presented)* A diagnostically or therapeutically labeled anti-angiogenic polypeptide comprising a polypeptide or variant according to claim 1 to which
 - (i) is conjugated a detectable diagnostic label or
 - (ii) is bound a therapeutically active moiety.
- 4.. *(previously presented)* A diagnostic HK-D3-related composition comprising:
 - (a) the detectably labeled polypeptide of claim 3; and
 - (b) a diagnostically acceptable carrier.
5. *(original)* The composition of claim 4 wherein the detectable label is selected from the group consisting of a radionuclide, a PET-imageable agent, an MRI-imageable agent, a fluorescer, a fluorogen, a chromophore, a chromogen, a phosphorescer, a chemiluminescer and a bioluminescer.
6. *(original)* The composition of claim 5, wherein the detectable label is a radionuclide selected from the group consisting of ^3H , ^{14}C , ^{35}S , ^{67}Ga , ^{68}Ga , ^{72}As , ^{89}Zr , ^{97}Ru , ^{99}Tc , ^{111}In , ^{123}I , ^{125}I , ^{131}I , ^{169}Yb and ^{201}Tl .
7. *(original)* The composition of claims 5 wherein the detectable label is a fluorescer or fluorogen selected from the group consisting of fluorescein, rhodamine, dansyl, phycoerythrin, phycocyanin, allophycocyanin, *o*-phthaldehyde, fluorescamine, a fluorescein derivative, Oregon Green, Rhodamine Green, Rhodol Green and Texas Red.
8. *(previously presented)* An anti-angiogenic pharmaceutical composition comprising:
 - (a) an anti-angiogenic effective amount of the polypeptide or variant of claim 1, and
 - (b) a pharmaceutically acceptable carrier.

9. (original) The pharmaceutical composition of claim 8 in a form suitable for injection.

10. (previously presented) A therapeutic anti-angiogenic pharmaceutical composition comprising:

- (a) an effective amount of the polypeptide of claim 3 to which the therapeutically active moiety is bound directly or indirectly; and
- (b) a therapeutically acceptable carrier.

11. (original) The therapeutic composition of claim 10 wherein the therapeutically active moiety is a radionuclide.

12. (original) The therapeutic composition of claim 11, wherein the radionuclide is selected from the group consisting of ^{47}Sc , ^{67}Cu , ^{90}Y , ^{109}Pd , ^{125}I , ^{131}I , ^{186}Re , ^{188}Re , ^{199}Au , ^{211}At , ^{212}Pb and ^{217}Bi .

13. (original) The therapeutic composition of claim 10 in a form suitable for injection.

14. (withdrawn/amended) A method for inhibiting cell migration, cell invasion, cell proliferation or angiogenesis, or for inducing apoptosis, comprising contacting cells associated with undesired cell migration, invasion, proliferation or angiogenesis with an effective amount of the polypeptide or variant of claim 1.

15. (withdrawn) A method for inhibiting cell migration, cell invasion, cell proliferation or angiogenesis, or for inducing apoptosis, comprising contacting cells associated with undesired cell migration, invasion, proliferation or angiogenesis with an effective amount of the therapeutically labeled polypeptide of claim 3.

16. (withdrawn) A method for treating a subject having a disease or condition associated with undesired cell migration, invasion, proliferation, or angiogenesis, comprising administering to the subject an effective amount of a pharmaceutical composition according to claim 8.

17. (withdrawn) A method for treating a subject having a disease or condition associated with undesired cell migration, invasion, proliferation, or angiogenesis, comprising administering to the subject an effective amount of a therapeutic composition according to claim 10.

18. (withdrawn) An isolated nucleic acid molecule that encodes the polypeptide or variant of claim 1.

19. (withdrawn/currently amended) The nucleic acid selected molecule of claim 18 selected from the group consisting of:

- (a) a nucleic acid having the sequence SEQ ID NO:4,
- (a[[b]]) a nucleic acid having the sequence SEQ ID NO:5,
- (b[[c]]) a nucleic acid having the sequence SEQ ID NO:6, and
- (c[[d]]) a nucleic acid having a sequence homologous to SEQ ID NO:4, 5 or 6 encoding a biologically active polypeptide that has at least 20% of the activity of native HK-D3 in inhibiting angiogenesis, endothelial cell proliferation or endothelial tube formation in an *in vitro* or *in vivo* bioassay.

20. (withdrawn) An expression vector comprising the nucleic acid of claim 18 operatively linked to

- (a) a promoter and
- (b) optionally, additional regulatory sequences that regulate expression of said nucleic acid in a eukaryotic cell.

21. (withdrawn) An expression vector comprising the nucleic acid of claim 19 operatively linked to

- (a) a promoter and
- (b) optionally, additional regulatory sequences that regulate expression of said nucleic acid in a eukaryotic cell.

22. (withdrawn) The expression vector of claim 20 which is a plasmid.

23. (withdrawn) The expression vector of claim 20 which is a viral vector.

24. (withdrawn) A cell transformed or transfected with the nucleic acid molecule of claim 18

25. (withdrawn) A cell transformed or transfected with the nucleic acid molecule of claim 19.

26. (withdrawn) A cell transformed or transfected with the expression vector of claim 20.

27. (withdrawn) A cell transformed or transfected with the expression vector of claim 21.

28. (withdrawn) The cell of claim 24 which is a mammalian cell.

29. (withdrawn) The mammalian cell of claim 28 which is a human cell.

30. (withdrawn/currently amended) A method for providing to a cell, tissue or organ an angiogenesis-inhibitory amount of HK-D3 (SEQ ID NO:1), HK-D3v (SEQ ID NO:3), or a ~~conservative amino acid substitution~~ variant thereof (SEQ ID NO:2), comprising administering to said cell tissue or organ, the expression vector of claim 18, such that the nucleic acid is taken up and expressed in said cell, tissue or organ.

31. (withdrawn) The method of claim 30 wherein said administering is *in vivo*.

32. (withdrawn/currently amended) A method for providing to a cell, tissue or organ an angiogenesis-inhibitory amount of HK-D3 (SEQ ID NO:1), HK-D3v (SEQ ID NO:3), or HK-d3v(GS) (SEQ ID NO:2), or ~~a conservative amino acid substitution variant thereof~~, comprising contacting said cell tissue or organ, with the transformed or transfected cells of claim 28 that express the polypeptide or variant.

33. (withdrawn) The method of claim 32 wherein said contacting is *in vivo*.

34. (withdrawn/amended) A method for inhibiting angiogenesis in a subject in need of such inhibition, comprising administering to the subject an effective amount of the expression vector of claim 20, such that said nucleic acid is expressed resulting in the presence of an angiogenesis-inhibiting amount of said polypeptide or variant, thereby inhibiting said angiogenesis.

35. (withdrawn) The method of claim 34 wherein said subject has a tumor, and said angiogenesis inhibition results in reduction in size or growth rate of said tumor or destruction of said tumor.

36. *(withdrawn/amended)* A method for inhibiting angiogenesis in a mammalian subject in need of such inhibition, comprising administering to the subject an effective amount of the transformed or transfected cells of claim 28, which cells produce and provide in the subject an angiogenesis-inhibiting amount of said polypeptide or variant, thereby inhibiting said angiogenesis.

37. *(withdrawn)* The method of claim 36 wherein said subject has a tumor, and said angiogenesis inhibition results in reduction in size or growth rate of said tumor or destruction of said tumor.

38. *(withdrawn)* The method of claim 34, wherein said subject is a human.

39. *(withdrawn)* The method of claim 36, wherein said subject is a human.

40. *(withdrawn/amended)* An affinity ligand useful for binding to or isolating an HK-D3-binding molecule or cells expressing the binding molecule, comprising the polypeptide or variant of claim 1 immobilized to a solid support or carrier.

41. *(withdrawn)* A method for isolating a HK-D3-binding molecule from a complex mixture comprising:

- (a) contacting the mixture with the affinity ligand of claim 40;
- (b) allowing material in the mixture to bind to the ligand;
- (c) removing unbound material from the ligand; and
- (d) eluting the bound HK-D3-binding molecule,

thereby isolating said HK-D3 binding molecule.

42. *(withdrawn)* A method for isolating or enriching cells expressing a HK-D3-binding site or receptor from a cell mixture, comprising

- (a) contacting the cell mixture with the affinity ligand of claim 40;
- (b) allowing any cells expressing the binding site or receptor to bind to the affinity ligand;
- (c) separating cells bound to the affinity ligand from unbound cells; and
- (d) removing the bound cells from the affinity ligand,

thereby isolating or enriching the HK-D3 binding site-expressing cells.